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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,699	10/02/2003	David Bar-Or	4172-85	2007

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EXAMINER	
EMCH, GREGORY S	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
12/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,699	BAR-OR ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/27/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Claims 47 and 51 have been amended in the reply filed on 27 August 2008. Claims 47-54 are pending and under examination in the instant office action.

Information Disclosure Statement

A signed and initialed copy of the IDS paper filed 27 August 2008 is enclosed in this action.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 47-54 under 35 U.S.C. 112, first paragraph, is maintained for reasons of record and as set forth below. This is because the specification, while being enabling for a method of diagnosing multiple sclerosis wherein the biological sample is serum, plasma or blood, does not reasonably provide enablement for the claimed method of monitoring multiple sclerosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

In the reply filed on 27 August 2008, Applicants assert that the claimed method can detect the presence or absence of active multiple sclerosis (MS) and that a single use of this method will allow the artisan to determine whether or not a patient is currently experiencing active MS. Applicants assert that the use of the claimed method over a period of time, on successive samples obtained from a single patient, will allow the skilled artisan to determine the number of active episodes of multiple sclerosis the patient experienced during that period of time. Applicants assert that this information could be used, for example, to determine whether treatments administered to the patient have served to eliminate active multiple sclerosis or to reduce the number, or frequency, of active multiple sclerosis episodes in that patient. Therefore, Applicants assert that through use of the claimed method, the skilled artisan could readily monitor multiple sclerosis in a patient.

Applicants' arguments have been fully considered and are not found persuasive. As stated previously, the claimed biomarkers, i.e., those with a mass of 175 and 145 are described only in terms of mass and can encompass a multitude of undisclosed compounds. Applicants' data in the specification provides a correlation between the

claimed markers and patients diagnosed with MS in a small sample size. Applicants have provided no data regarding the claimed embodiment of monitoring MS disease. Again, the art does not provide compensatory teachings as it is completely silent with regards to this embodiment. Moreover, the art teaches that diagnosis of MS is unpredictable. For example, Bielekova et al. (cited previously) teaches, "multiple sclerosis is a complex disease, as several pathophysiological processes (including inflammation, demyelination, axonal damage and repair mechanisms) participate in the disease process. Furthermore, as new pathological evidence reveals, these processes are not uniformly represented across patient populations but can selectively predominate in individual patients, thus contributing to the heterogeneity in phenotypic expression of the disease, its prognosis and response to therapies" (Abstract). The reference also teaches that "In multiple sclerosis, the situation is further complicated by the fact that the disease pathophysiology is complex and the applied therapy may positively influence only one of the contributing processes (e.g. effect of immunosuppressive therapies on inflammation) and have no effect, or potentially have even negative influence on others" (p.1464). Thus, even with further clinical measures, given the art-accepted unpredictable nature of diagnosing or detecting MS, one could not be reasonably assured that the claimed invention would be capable of monitoring the disease. Additional factors would be required to practice the method of monitoring MS, as evidenced by the Bielekova et al. reference, and therefore, a person skilled in the art would recognize that monitoring MS in humans according to the claims as highly problematic (see MPEP §2164.03). Thus, given the lack of guidance in the art and the

specification with regards to monitoring of MS, there is no nexus established between Applicants' data and monitoring of MS.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Due to the large quantity of experimentation necessary practice the claimed method of monitoring MS, given the lack of direction/guidance presented in the specification, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the claimed methods, and the breadth of the claims, undue experimentation would be required of the skilled artisan to practice the claimed invention commensurate in scope with the claims.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G.E./

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
08 December 2008

/Jeffrey Stucker/
Supervisory Patent Examiner, Art Unit 1649